UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/578,363	05/25/00	WALLNER	B I0248/7012

HM22/0629

EDWARD R GATES
WOLF GREENFIELD & SACKS PC
600 ATLANTIC AVENUE
BOSTON MA 02210

EXAMINER	
RUSSEL,J	
ART UNIT	PAPER NUMBER
1653	8

DATE MAILED:
06/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

BEST AVAILABLE COPY

Office Action Summary

Application No.	Applicant(s)
09/578,363	B. Wallner et al
Examiner	**Group Art Unit**
J. Russel	1653

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 5-25-2000 and 9-19-2000.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-8, 11-19, 31, 36, and 37 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-8, 11-19, 31, 36, and 37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5, 6, 7

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Acti n Summary

1. The disclosure is objected to because of the following informalities: The status of all U.S. patent applications referred to in the specification (see especially page 34, line 22) should be updated. Appropriate correction is required.

2. Claims 1-8, 11-17, 19, 31, 36, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 19, 36, and 37 are indefinite because they do not recite what constitutes Formula I. To the extent that Applicants may be relying on the disclosure of Formula I in the specification, it should be noted that claims are to be complete in and of themselves. Applicants have not shown that there is no practical way to insert the definition of Formula I into the claims. See MPEP 2173.05(s).

3. Claim 7 is objected to because of the following informalities: At claim 7, line 2, a comma should be inserted after "ovarian cancer". Appropriate correction is required.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 11-19, 31, 36, and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 09/374,724 Although the conflicting claims are not identical, they

are not patentably distinct from each other because the claims of the '724 application anticipate instant claims 1, 2, 15, and 18. Note that claim 13 of the '724 application recites the treatment of neoplasms, tumors, or cancers. With respect to instant claim 19, because the subject, the active agent, and the method steps are the same in the claimed method of the '724 application as are claimed by Applicants, inherently angiogenesis will be inhibited in the claimed method of the '724 application to the same extent claimed by Applicants. With respect to instant claims 12-14, 31, 36, and 37, it would have been obvious to one of ordinary skill in the art to combine the chemotherapeutic method claimed in the '724 application with other known methods of treating neoplasms, tumors, or cancers, including surgery or treatment with other anti-cancer compounds, because it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer. With respect to instant claims 11, 16, and 17, it would have been obvious to one of ordinary skill in the art to treat neoplasms, tumors, or cancers in the claimed method of the '724 application in any subject with neoplasms, tumors, or cancers, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat neoplasms, tumors, or cancers in any patient in which they are found and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the claimed method of the '724 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Instant claims 1-8, 11-19, 31, 36, and 37 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/135,861 because the

provisional application, under the test of 35 U.S.C. 112, first paragraph, is deemed to disclose the instant claimed invention.

Because copending application 09/374,724 currently does not have a claim for priority under 35 U.S.C. 119(e), the '724 application is not provisionally available as prior art under 35 U.S.C. 102(e) against instant claims 1-8, 11-19, 31, 36, and 37. If the '724 application is amended to include a claim for priority under 35 U.S.C. 119(e), then the examiner will have to reconsider this issue and, if necessary, will make all appropriate rejections under 35 U.S.C. 102(e) and/or 103.

It should also be noted that to the extent that the instant claims might be amended in the future, especially with respect to any definition of formula I which might be inserted into the instant claims, the examiner will have to reconsider the above analysis as to whether the claims as amended are entitled under 35 U.S.C. 119(e) to the benefit of the filing date of the provisional application.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

7. Claims 1, 2, 15, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Powers et al (U.S. Patent No. 5,543,396). Powers et al teach the use of DPP-IV inhibitors to control tumor invasion. See, e.g., column 1, lines 13-22 and 54-57; column 3, lines 19-24; and column 16, lines 11-15. The inhibitors of Powers et al satisfy Applicants' Formula I as defined in the specification. Because the subject, the active agent, and the method steps are the same in Powers et al as are claimed by Applicants, inherently angiogenesis will be inhibited in Powers et al to the same extent claimed by Applicants.

8. Claims 11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being obvious over Powers et al (U.S. Patent No. 5,543,396). Application of Powers et al is the same as in the above rejection of claims 1, 2, 15, and 19. Powers et al do not describe the subjects being treated to control tumor invasion as being otherwise free of symptoms calling for hemopoietic stimulation,

as having normal hemopoietic activity, or as being HIV negative. However, Powers et al do not set forth any limitations on the type of subjects who can be treated to control tumor invasion. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to control tumor invasion according to the method of Powers et al in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to control tumor invasion in any patient in which tumors are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of Powers et al.

9. Claims 12-14, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Powers et al (U.S. Patent No. 5,543,396) as applied against claims 1, 2, 15, and 19 above, and further in view of O'Reilly et al or Brooks et al. Powers et al do not disclose combining their DPP-IV inhibitors with other anti-cancer or anti-angiogenic compounds in the treatment of tumor invasion, and do not disclose practicing their method in combination with surgical methods of tumor treatment. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the tumor treatment of Powers et al with other known methods of treating tumors, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer.

10. Claims 1, 2, 5, 7, 15, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kinder et al (U.S. Patent No. 4,963,655). Kinder et al teach treating tumors by administering protease inhibitors comprising boronic acid analogs of amino acids. Tumors to be treated include melanoma, human lung carcinoma, and murine leukemia. See, e.g., the abstract; and column 2, lines 44-63. In view of the similarity in structure and functional between the inhibitors of Kinder et al and Applicants' compounds of Formula I, the inhibitors of Kinder et al are deemed inherently to comprise a targeting group which binds to the reactive site of FAP-α or other post proline-cleaving enzyme and to comprise a reactive group capable of reacting with a functional group in FAP-α or other post proline cleaving enzyme. Sufficient evidence of similarity is deemed to be present between the inhibitors of Kinder et al and Applicants' compounds of Formula I to shift the burden to Applicants to provide evidence that their compounds of Formula I are unobviously different than the inhibitors of Kinder et al. Because the subject, the active agent, and the method steps are the same in Kinder et al as are claimed by Applicants, inherently angiogenesis will be inhibited in Kinder et al to the same extent claimed by Applicants.

11. Claims 11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being obvious over Kinder et al (U.S. Patent No. 4,963,655). Application of Kinder et al is the same as in the above rejection of claims 1, 2, 5, 7, 15, and 19. Kinder et al do not describe the subjects being treated for tumors as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. However, Kinder et al do not set forth any limitations on the type of subjects who can be treated to control tumor invasion. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made

to treat tumors according to the method of Kinder et al in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat tumors in any patient in which tumors are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of Kinder et al.

12. Claims 12-14, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Kinder et al (U.S. Patent No. 4,963,655) as applied against claims 1, 2, 5, 7, 15, and 19 above, and further in view of O'Reilly et al or Brooks et al. Kinder et al do not disclose combining their inhibitors with other anti-cancer or anti-angiogenic compounds in the treatment of tumors, and do not disclose practicing their method in combination with surgical methods of tumor treatment. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the tumor treatment of Kinder et al with other known methods of treating tumors, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer.

13. Claims 1, 2, 4-7, 15, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 95/15309. The WO Patent Application '309 teaches preventing the metastases of breast and prostate tumors to the lungs by administering DP-IV inhibitors. See, e.g., the abstract and page 3, lines 10-11 and 17-18. Breast and prostate tumors are epithelial in

origin. Because the subject, the active agent, and the method steps are the same in the WO Patent Application '309 as are claimed by Applicants, inherently angiogenesis will be inhibited in the WO Patent Application '309 to the same extent claimed by Applicants.

14. Claims 11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/15309. Application of the WO Patent Application '309 is the same as in the above rejection of claims 1, 2, 4-7, 15, and 19. The WO Patent Application '309 does not describe the subjects being treated for tumors as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. However, the WO Patent Application '309 does not set forth any limitations on the type of subjects who can be treated for breast and prostate tumors and to prevent metastases. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat breast and prostate tumors and to prevent metastases according to the method of the WO Patent Application '309 in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat breast and prostate tumors and to prevent metastases in any patient in which tumors are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of the WO Patent Application '309.

15. Claims 12-14, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/15309 as applied against claims 1, 2, 4-7, 15, and 19 above, and further in view of O'Reilly et al or Brooks et al. The WO Patent Application '309 does not disclose combining their inhibitors with other anti-cancer or anti-angiogenic compounds in the treatment of tumors, and do not disclose practicing their method in combination with surgical

methods of tumor treatment. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the tumor treatment of the WO Patent Application '309 with other known methods of treating tumors, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer.

16. Claims 1-8, 15, and 18 are rejected under 35 U.S.C. 103(a) as being obvious over Zimmerman et al (U.S. Patent No. 5,767,242) in view of Bachovchin (U.S. Patent No. 5,965,532). Zimmerman et al teach treating cancer associated with reactive stromal fibroblasts, including epithelial cancers such as breast, lung, pancreatic, and colorectal cancers, and including bone and soft tissue sarcomas, by inhibiting FAP-α (see, e.g., column 1, line 37 - column 2, line 16, and column 11, line 9 - column 12, line 8). Zimmerman et al also disclose that FAP-α comprises three segments corresponding to highly conserved catalytic domains characteristic of serine proteases such as DPPIV (see, e.g., column 5, lines 38-33, and Table 2). Zimmerman et al do not teach using as an FAP-α inhibitor a compound of Applicants' Formula I or a compound such as Val-boro-Pro. Firstly, because the most common structure for an enzyme inhibitor is a ligand bound to a reactive group, it would have been obvious to use an inhibitor of such a structure (i.e. the structure of Applicants' Formula I) to inhibit FAP-α in the method of Zimmerman et al in order to treat cancer. Secondly, because of the analogous structures of FAP-α and DPP-IV, and because inhibitors of one enzyme are commonly used to inhibit other

enzymes which are members of the same class, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made use Val-boroPro, which Bachovchin teaches is a known inhibitor with the highest affinity for DPP-IV (see, e.g., column 3, lines 13-34), to inhibit FAP-α and thereby treat cancer according to the method of Zimmerman et al.

17. Claims 11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being obvious over Zimmerman et al (U.S. Patent No. 5,767,242) in view of Bachovchin (U.S. Patent No. 5,965,532). Application of Zimmerman et al and Bachovchin is the same as in the above rejection of claims 1-8, 15, and 18. Zimmerman et al do not describe the subjects being treated for cancer as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. However, Zimmerman et al do not set forth any limitations on the type of subjects who can be treated for cancer. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat breast and prostate tumors and to prevent metastases according to the method of Zimmerman et al as modified above by Bachovchin in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat cancer in any patient in which tumors are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of Zimmerman et al in view of Bachovchin, and because Zimmerman et al's proposed mechanism for treatment is independent of a patient's hemopoietic activity or HIV status.

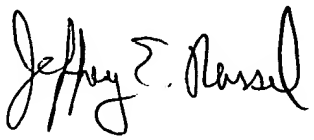
18. Claims 12-14, 19, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Zimmerman et al (U.S. Patent No. 5,767,242) in view of Bachovchin (U.S. Patent No. 5,965,532) as applied against claims 1-8, 15, and 18 above, and further in view of O'Reilly et al

or Brooks et al. Zimmerman et al do not disclose combining their inhibitors with other anti-cancer or anti-angiogenic compounds in the treatment of tumors, and do not disclose practicing their method in combination with surgical methods of tumor treatment. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the cancer treatment of Zimmerman et al as modified above by Bachovchin with other known methods of treating tumors, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer.

19. With respect to the Information Disclosure Statement filed October 2, 2000, the upper-right hand corner of the listing recites 'Page 1 of 8"; however, the examiner found only a single page of listed references. If there were actually eight pages of references listed, Applicants are requested to re-supply the complete listing with copies of the cited references so that the examiner can consider them and make them of record.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1653

JRussel

June 28, 2001